(b) contacting the substance with the recombinant opioid receptor polypeptide; and

(c) detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide.

72. (Amended) The process of claim 65, wherein detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide involves measuring (i) the ability of the recombinant opioid receptor polypeptide to bind the candidate substance; (ii) ability of the candidate substance to activate ion channels in a cell membrane; or (ii) modulation of ion channels in the cell membrane of part (ii).

74. (Amended) A process for screening a candidate substance for its ability to bind to an opioid receptor comprising:

(a) expressing a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 35 contiguous bases of SEQ ID NO:7, including the guanine nucleotide at position 389 of SEQ ID NO:7;

(b) contacting the candidate substance with the recombinant opioid receptor polypeptide; and

(c) detecting the ability of the candidate substance to bind to the recombinant opioid receptor polypeptide.

II. RESPONSE TO OFFICE ACTION

A. Status of the Claims

This application is a divisional of USN 08/889,108 filed on July 7, 1997, which is a file-wrapper continuation of USN 08/305,518 filed on September 13, 1994, which is a continuing application of USN 08/120,601 filed on September 13, 1993, which is continuing application of U.S. Serial No. 08/056,886 filed on March 8, 1993. A copy of an Inventor's Declaration claiming priority to U.S. Serial No. 08/056,886 is included herewith. After a Preliminary Amendment and Response to Office Action on April 6, 2001, claims 44-47, 65-74, and 76-82

were pending and subsequently rejected by the Office Action mailed July 17, 2001 ("the Action"). Herein, claims 44, 46, 47, 6572, and 74 are amended (see Appendix A). Support for the amendments can be found in the Specification at least at page 71, lines 11-19. Thus, no new matter has been added.

Claims 44, 46, 47, 65, 67-74, and 76-82 are the subject of this response. A copy of the pending claims is provided in Appendix B.

B. Amendment to Specification

The Specification has been amended to correct minor errors in amendment to the Specification filed in the Preliminary Amendment of July 27, 2000. Appendix C shows the amendment to the Specification.

C. Claims 44-47 and 65-82 Are Adequately Described

The Action rejects claims 44-47 and 65-82 under 35 U.S.C. § 112, first paragraph, as lacking written description. The ground for this rejection is based on the term "interact" because, as stated in the Office Action mailed December 6, 2000, the application does not adequately describe "all of the possible interactions of a candidate substance with the mu opioid receptor of the invention." The Examiner also previously pointed out that the term "interact" can refer to a compound that has a direct interaction with the receptor, such as binding, or the term could refer to a compound that interacts indirectly with the claimed receptor. The present Action adds that the definition for "interact with" includes the phrase "other intramolecular interactions," which is alleged not to be adequately described in the specification. Applicant traverses this rejection.

The written description requirement is whether the "description clearly allows persons of ordinary skill in the art to recognize that he or she invented what is claimed." MPEP 2163.02 (citing *In re Gosteli*, 872 F.2d 1008, 1012, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989)). The standard is not, as contended in the Action, that *all* possible ways of satisfying a term be provided. This is simply not the correct standard. However, in the interest of expediting prosecution of this case, Applicant is amending the claim to recite "bind to," but reserves the right to prosecute a claim reciting "interact with" in a continuation application at a later date. Accordingly, this rejection should be withdrawn in this case.

D. Claim 44 Is Definite

Claim 44 has also been rejected as indefinite. The ground for this rejection is based on the word "interact." While Applicant strongly disagrees with this rejection as well, contending that the word has been used according to its plain and ordinary meaning, in the interests of expediting the prosecution of this case, the phrase "interact with" has been replaced with "bind to." Applicant respectfully requests the rejections under 35 U.S.C. § 112 be withdrawn.

E. Claims Are Not Anticipated

1. Fukuda *et al.* Is Not Prior Art

The Action rejects claims 44-47 under 35 U.S.C. § 102 (b) as being anticipated by Fukuda *et al.*, which was published in the August 1993 volume of FEBS Letters ("Fukuda 1993 reference"). The Fukuda 1993 reference is said to teach a protein that is 100% identical to SEQ ID NO:2 and a method of determining the binding of ligands to the expressed receptor. Applicant traverses this rejection.

First, Applicant notes that the present application claims priority to Serial Number 08/305,518 filed on September 13, 1993 ("the '518 application). This parent application contains SEQ ID NO:2 (p. 92) and discloses that the "present invention contemplates a process of screening substances for their ability to interact with a mu opioid receptor polypeptide. . . ." '518 Specification at page 15. Furthermore, in Example II binding studies are done on the cloned rat opioid receptor. '518 Specification at pages 78-79. Thus, the present application has an effective filing date with respect to the teaching of the Fukuda 1993 reference at least as early as September 13, 1993. Accordingly, the Fukuda reference cannot be prior art under 35 U.S.C. § 102 (b) because it was not published more than one year prior to the effective filing date of the present application.

To the extent that the Fukuda 1993 reference is prior art under 35 U.S.C. § 102 (a), the Declaration of Lei Yu, Regarding Chen and Fukuda 1993 Reference included herewith (Appendix D) shows that the Applicant invented SEQ ID NO:2 and its use in binding studies at least as early as the preceding Chen reference, which was published in the July 1993 volume of Molecular Pharmacology and submitted on May 4, 1993. Thus, this declaration provides evidence that the applicant had in his possession, in this country, at least as much as much as the Fukuda 1993 reference showed, as is demonstrated by the Chen reference. Accordingly, the Fukuda 1993 reference also does not qualify as prior art under 35 U.S.C. § 102 (a). *See In re Stempel*, 1193 U.S.P.Q. 77 (C.C.P.A. 1957). Applicant respectfully requests this rejection be withdrawn.

2. Wang *et al.* Does Not Anticipate Claims 65-70, 72-74, 76-80, and 82

The Action also rejects claims 65-70, 72-74, 76-80, and 82 under 35 U.S.C. § 102 (b) as being anticipated by Wang *et al.* ("Wang reference"). The Wang reference is said to teach a

recombinant opioid receptor that is at least 100 nucleotides in length and which comprises guanine 389 (Sequence Comparisons B and C). The Action also contends that the Wang reference discloses methods of determining the ability of ligands to interact with this receptor. Applicant traverses this rejection.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). The Action asserts there is identity, however, a closer look at the reference shows that the sequence disclosed in the Wang reference does not teach a recombinant opioid receptor that is 100 nucleotides in length and that includes guanine 389. In Fig. 1 of the Wang reference, the predicted amino acid sequence for a human μ opioid receptor (hMOR1) is provided. In line 2 of the human sequence, at amino acid residue 51, there is an "N" for asparagine. The amino acid at that same position in the sequence of the invention is an aspartate. SEQ ID NO:2 and Specification at page 121, lines 20-25. Furthermore, the GenBank accession number identified in the legend to Fig. 1 is L25119 (Appendix E). That sequence, included herewith, does not have a guanine at the position corresponding to position 389 in SEQ ID NO:7. Instead, there is a "A" instead of a "G" at that corresponding position, as indicated by the arrow, which is part of the codon AAC encoding asparagine, instead of GAC encoding aspartic acid. (*See* Appendix E codon chart).

Because the Wang reference does not meet each element of the claim because it does not teach a nucleic acid sequence with a guanine at position 389 of SEQ ID NO:7, it cannot anticipate the claims. Furthermore, there is no suggestion or motivation to replace the cytosine at that position with a guanine, particularly since this changes the encoded amino acid residue

from an asparagine to an aspartate. Consequently, the Wang reference also does not render the claims obvious. Applicant respectfully requests this anticipation rejection be withdrawn.

F. Claims Are Not Anticipated or Rendered Obvious by Chen *et al.*

The Action also claims 44-47 under 35 U.S.C. § 103 (a) as being unpatentable over Chen *et al.* ("Chen reference").[1] It contends that the Chen reference teach nucleic acids encoding proteins that are 100% identical to SEQ ID NO:2 and 4. Applicant respectfully traverses this rejection.

As discussed above, the Declaration of Lei Yu, Regarding the Chen and Fukuda 1993 Reference is submitted herewith (Appendix D). This declaration removes the Chen reference as prior art under 35 U.S.C. § 102 (a). In his declaration, Dr. Yu sets forth that the non-inventors of the Chen reference—Yan Chen, Anton Mestek, Jian Liu, and Joyce Hurley—are not inventors of the claimed subject matter. These non-inventors were researchers in Dr. Yu's laboratory. They performed tasks related to the creation of the claimed subject matter under the direction and control of Dr. Yu. They did not participate in the conception of the subject matter claimed in the present application. In view of this, they are not properly listed as inventors on the application.

Lei Yu is the only co-author of the Chen reference who is properly an inventor; therefore, the reference, is not § 102(a) prior art. *In re Katz* 215 U.S.P.Q. 14 (C.C.P.A. 1982). The Chen reference was published less than a year before the priority date of the present application; therefore, it is not § 102 (b) prior art. Because the Chen reference is not prior art, it cannot

[1] The rejection of claims 44-47 over the Chen reference was stated in the Action to be under 35 U.S.C. § 103(a) but the rejection was placed under the heading of rejections under 35 U.S.C. § 102. Because the Chen reference is not prior art, neither rejection is appropriate.

provide the basis for either an anticipation rejection under § 102 or an obviousness rejection under § 103. Accordingly, Applicant respectfully requests this rejection be withdrawn.

G. Claims Are Not Rendered Obvious by the Fukuda References

The Action rejects claims 44-47 under 35 U.S.C. § 103(a) as being unpatentable over Fukuda *et al.*, FEBS Letters 343:42-46, 1994 ("the Fukuda 1994 reference") in view of the Fukuda 1993 reference discussed earlier. The Fukuda 1994 reference is alleged to teach a protein that is 100% identical to SEQ ID NO:17 and the Fukuda 1993 reference is said to teach a method of determining the binding of ligands to the expressed receptor. Applicant respectfully traverses this rejection.

A Declaration of Lei Yu, Ph.D, Regarding the Fukuda 1994 Reference is submitted herewith (Appendix F). This declaration is similar to a declaration previously submitted on October 15, 1996 in the parent application, USN 08/305,518. In this Declaration, the inventor sets forth that he had cloned and sequenced cDNA encoding the sequence of SEQ ID NO:17 prior to the April 18, 1994 publication date of the Fukuda 1994 reference. Because the Fukuda 1994 reference reports the same polypeptide sequence as earlier cloned by Lei Yu, it cannot be prior art with respect to the sequence the Action purports it to teach.

Furthermore, the Fukuda 1994 reference contains no nucleic acid sequence for the reported polypeptide. Therefore, it cannot anticipate or render obvious claims specifically directed to the polynucleotide sequence of all or part of SEQ ID NO:17.

The earlier 1993 Fukuda reference is cited as teaching a method of determining the binding of ligands to an expressed receptor. The other declaration of Lei Yu is offered to show that the Fukuda 1993 reference is not prior art as well with respect to its alleged teaching. The

declaration sets out that Dr. Yu cloned an opioid receptor and characterized it by evaluating the ability of the receptor to bind ligands. To this extent, the Fukuda 1993 reference is also not proper prior art.

Consequently, because neither the Fukuda 1994 reference nor the Fukuda 1993 references is prior art, Applicant respectfully requests this rejection be withdrawn.

H. Sequence Submission of Bare Is Not Prior Art

In the interests of expediting the prosecution of this case, Applicant submits the Declaration of Lei Yu, Regarding the Bare Sequence Submission (Appendix G). The Bare sequence submission is not the basis for any rejection. It is identified in Sequence Comparisons A and B provided with the Action with respect to the rejection based on the Wang reference (Section C.2 *infra*). The declaration provides evidence that the inventor invented the cDNA sequence of the entire human μ opioid receptor prior to any purported July 24, 1994 submission by Lane A. Bare as GenBank accession number HSU12569. Thus, the sequence submission of Bare is not proper prior art against the above-referenced patent application.

I. Conclusion

The Examiner is invited to contact the undersigned attorney at 512-536-3081 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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Date: October 17, 2001